

Lecture 25: Functional proteomics and proteome database

FUNCTIONAL PROTEOMICS

Genome of an organism certainly provides a wealth of information. As recently several genomes have been sequenced, the current challenge has been shifted to study function of all proteins coded by genome (proteome). The goal of proteome research is not easy because many difficulties were faced when moving from genome to proteome research. Genome is comparatively static in nature than proteome of an organism; protein expression profiles change several times during the cell cycle and are heavily affected by a number of intracellular and extracellular stimuli (temperature, stress, apoptotic signals, etc.). The size and complexities of proteome is much larger than genome because of phenomenon like alternative splicing and post-translational modifications.

Proteome research is essentially focused on two major areas:

- Expression proteomics: Study of up-regulation and down-regulation of protein levels
- Functional proteomics: Study of protein activities/functions, characterization of multi-protein complexes, and role of proteins in signalling pathways.

With increase in the number of genome sequencing projects, there is a concomitant exponential growth in the number of protein sequences whose function is still unknown. The functional proteomics approaches are used to study biological functions of unknown proteins at the molecular level. In cells, many proteins display their biological functions in network (protein-protein interaction) as protein complexes. Functional proteomics is also involved in unravelling such protein-protein interactions and function of protein complexes. **We have already studied methodologies used in functional proteomics during earlier lectures of the course. For example:**

- **Protein identification by mass spectrometry methodologies. Once protein is identified, function of the protein may be predicted (explained in detail during lecture 17)**
- **Methods for Protein- Protein Interaction studies are already explained in lecture 20.**

Reference and further reading



Clinica Chimica Acta 357 (2005) 140–150



Functional proteomics

Maria Monti, Stefania Orrù, Daniela Pagnozzi, Piero Pucci*

*CEINGE Biotechnologie Avanzate scari and Dipartimento di Chimica Organica e Biochimica, Università di Napoli Federico II, via Comunale Margherita 482, Naples 80145, Italy*Received 4 March 2005; accepted 9 March 2005
Available online 8 June 2005

Abstract

Background: With the increase in the number of genome sequencing projects, there is a concomitant exponential growth in the number of protein sequences whose function is still unknown. Functional proteomics constitutes an emerging research area in the proteomic field whose approaches are addressed towards two major targets: the elucidation of the biological function of unknown proteins and the definition of cellular mechanisms at the molecular level.

Methods: The identification of interacting proteins in stable complexes *in vivo* is essentially achieved by affinity-based procedures. The basic idea is to express the protein of interest with a suitable tag to be used as a bait to fish its specific partners out from a cellular extract. Individual components within the multi-protein complex can then be identified by mass spectrometric methodologies.

Results and conclusions: The association of an unknown protein with partners belonging to a specific protein complex involved in a particular mechanism is strongly suggestive of the biological function of the protein. Moreover, the identification of protein partners interacting with a given protein will lead to the description of cellular mechanisms at the molecular level. The next goal will be to generate animal models bearing a tagged form of the bait protein.

© 2005 Elsevier B.V. All rights reserved.

PROTEOME DATABASE

The field of proteomics deals with the global analysis of the total protein content (proteome) of an organism, a tissue or a cell type during various developmental stage and environmental conditions. Due to recent developments in high throughput techniques, proteomics research has gained momentum. The gap which exists between genomics and understanding cellular behaviour can be filled by proteomics.

As we have studied during earlier lectures, two dimensional gel electrophoresis (2D PAGE) is the specific technique for analysis of the whole protein expression profile of a given cell type or organism, under a set of specific conditions. In 2D PAGE, proteins in a sample are separated according to both isoelectric point (pI) and molecular weight (Mw), by a combination of isoelectric focusing and electrophoresis, respectively. Thus, 2D PAGE gel is characteristic of an organism at a given developmental stage and environmental condition. An ideal proteome data includes 2D PAGE gel image of an organism. This data may be available as tissue specific and developmental stage specific. Moreover, known functions/putative functions of all proteins of an organism are also mentioned. Moreover, all possible protein-protein interaction networks are also provided in many proteome databases.

Few Internet resources available:

Database	URL	Organism. Organelle/phenotype
Aarhus 2DPAGE Database	http://biobase.dk/cgi-bin/cells	Human(Skin biology, bladder cancer, fibroblast), mouse(kidney)
Aberdeen 2D PAGE	http://www.abdn.ac.uk/~mmb023/2dhome.htm	<i>Haemophilus influenza</i>
Cyano2Dbase	http://www.kazusa.or.jp/cyano/cyano2D	<i>Synechostic cyanobacteria</i>
ES cell-2D PAGE	http://www.dey.ac.uk/~dbl0nh I/2DPAGE	Embryonal stem cells
Harefield HSC 2D PAGE	http://www.harefeild.nthames.nhs.uk/nhil/protein	Human (heart, endothelial cells), rat(heart), dog (heart)
Maize genome database	http://moulon.moulon.inra.fr	Maize
SSI-2DPAGE	http://www.ssi.dk/en/forskning/tbimmun/ tbjemme.htm	<i>M.tuberculosis</i>
Proteome database system	http://www.mpiib-berlin.mpg.de/2D-PAGE/	

Home assignment

Do a survey about available online resources of Proteome database. How these databases are useful?

Submit your assignment to course developer by e-mail; you will get an e-mail reply with grading and feedback in a week time.